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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/579,248	02/28/2007	Elliot Altman	235.00550101	7812

26813 7590 06/16/2008

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EXAMINER	
DUFFY, PATRICIA ANN	
ART UNIT	PAPER NUMBER
1645	

MAIL DATE	DELIVERY MODE
06/16/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/579,248	ALTMAN ET AL.	
	Examiner	Art Unit	
	Patricia A. Duffy	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 March 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8,21-29,32-38 and 42* is/are pending in the application.

4a) Of the above claim(s) *36-38 and 42* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8, 21-29, 32-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12 May 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2006, 2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The response filed 3-3-08 has been entered into the record. Claims 1-8, 21-29, 32-38 and 42 are pending.

Drawings

The drawings in this application have been accepted. No further action by Applicant is required.

Specification

The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Information Disclosure Statement

The information disclosure statements filed in 2006 and 2007 have been considered. Initialed copies are enclosed.

Election/Restrictions

Applicant's election of Group I, specie peptide in the response filed 3-3-08 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 36-38 and 42 are withdrawn from consideration as drawn to a non-elected invention.

Claim Objections

Claim 21 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The claim recites that the peptide of peptidomimetic is conjugated to a bioactive compound. Since the peptide/peptidomimietic is already conjugated to biotin, a bioactive compound, this claim is seen to broaden the scope of the claims as it neither further limits the peptide/peptididomimetic or biotin of claim 1.

Claim Rejections - 35 USC § 102 or 103

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-8, 21-26 and 32 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Low et al (WO 90/12096, published October 18, 1990; of record).

Low et al teach transmembrane transport of exogenous molecules including proteins and polynucleotides in plant, mammalinan and bacterial/prokaryotic cells. Low et al teach that the method takes advantage of the location and multiplicity of biotin receptors on the membrane surfaces of most cells and the associated receptor mediated transmembrane processes (pages 4-5 of disclosure). The method comprises the step of contacting the membrane with the exogenous molecule complexed with a ligand consisting of biotin, biotin-receptor binding ligands for a time sufficient to permit transmembrane transport of the ligand complex and is useful and effective in all living cells that have biotin receptors associated with their cellular membranes (page 7 of disclosure). Low et al teaches suitable exogenous molecules including peptides, oligopeptides, proteins, antibodies, haptens, toxins, antibiotics including cephalosporins, penicillin, various therapeutics, vitamins, mineral and nutritional additives, nucleotides, oligonucleotides (pages 9-11 of disclosure). Low et al exemplifies biotin conjugated to various proteins was taken up by mammalian and plant cells in the absence of a membrane permeablizing agent. Low et al exemplifies biotin conjugated to plasmid DNA (pUC8) was added to *E. coli* that was made competent with the addition of MgCl2 and CaCl2, but in the absence of a

membrane permeabilizing agent. The antimicrobial effect on the cell was determined by the addition of ampicillin to the transformed cell culture. Colonies that survived the ampicillin treatment were counted.

Since the peptidomimetic of the claims has no specific structure, the claims as drawn to a peptidomimetic are anticipated by the art.

Claims 1-8, 22-26, 29 and 32-35 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Dargis et al (Antimicrobial Agents and Chemotherapy, 38(5):973-980, 1994; of record).

Dargis et al teach biotin linked beta lactam antibiotics, including ampicillin, 6-aminopenicillanic acid and 7-aminocephalosporanic acid (see abstract). Dargis et al teach contacting *E. coli* and *H. influenzae* (gram negative microorganisms) with Bio-amp and determining the biological activity thereof (see page 975, column, Results first full paragraph to page 976, column 2 and Figure 5 and Figure 9). Beta lactam antibiotics are known to kill bacteria (see page 973, column 1, first full paragraph). Inasmuch as, beta-lactam antibiotics kill gram negative bacterial cells, they necessarily inhibit the growth thereof because dead cells do not grow. As such, Dargis et al anticipates the instantly claimed invention.

Claim 1-8, 21-26, 29 and 32-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Low et al (WO 90/12096, published October 18, 1990).

Low et al teach transmembrane transport of exogenous molecules including proteins and polynucleotides in plant, mammalinan and bacterial/prokaryotic cells. Low et al teach that the method takes advantage of the location and multiplicity of biotin receptors on the membrane surfaces of most cells and the associated receptor mediated transmembrane processes (pages 4-5 of disclosure). The method comprises the step of contacting the membrane with the exogenous molecule complexed with a ligand consisting

of biotin, biotin-receptor binding ligands for a time sufficient to permit transmembrane transport of the ligand complex and is useful and effective in all living cells that have biotin receptors associated with their cellular membranes (page 7 of disclosure). Low et al teaches suitable exogenous molecules including peptides, oligopeptides, proteins, antibodies, haptens, toxins, bacteriocidal and bacteriostatic antibiotics including cephalosporins, penicillin, various therapeutics, vitamins, mineral and nutritional additives, nucleotides, nucleosides, oligonucleotides (pages 9-11 of disclosure). Low et al exemplifies biotin conjugated to various proteins was taken up by mammalian and plant cells in the absence of a membrane permeablizing agent and in the absence of CaCl2. Low et al exemplifies biotin conjugated to plasmid DNA (pUC8) was added to *E. coli* (an art recognized pathogen) that was made competent with the addition of MgCl2 and CaCl2, but in the absence of a membrane permeabilizing agent. The antimicrobial effect on the cell was determined by the addition of ampicillin to the transformed cell culture. Colonies that survived the ampicillin treatment were counted. Low et al differs by not exemplifying peptides and antibiotics conjugated to biotin for transport and detecting the antimicrobial activity thereof.

It would have been *prima facie* obvious to one having ordinary skill in the art at the time that the invention was made to substitute biotin-linked antimicrobial peptides, peptide antibiotics or antibiotics of Low et al for the pUC8 nucleic acid in the method of delivery to *E. coli* Low et al in the absence of CaCl2 because Low et al teach that biotin mediated transport is effective for delivery of any of the desired exogenous compounds and proteins and peptides in particular in the absence of CaCl2 and it would have been obvious to further test for the antimicrobial activity of the delivered compounds as a means of accessing the effectiveness of delivery of antimicrobial agents.

Claims 27 and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Low et al (WO 90/12096, published October 18, 1990) as applied to claims 1-8, 21-26, 29

and 32-35 above, and further in view of Kim (US Patent No 6,322,788 issued November 27, 2001).

The combination of Low et al is set forth supra. The combination differs by not further conjugating the biotin-antibiotic conjugate to an antibody that targets gram negative bacteria.

Kim teaches anti-bacterial antibodies conjugated to antibiotics including polymyxins, penicillins, cephalospornis. Kim teaches that the antibiotic-antibody conjugate should be such that it breaks after a shot time in the microenvironment of the infection site. Kim teaches that the advantage of the antibiotic conjugate is that the antibody targeting moiety provides for concentrated localized delivery of the antibiotic and higher dosages of antibiotics could be used without the degree of side effects of the unconjugated antibiotics (see columns 7-8, column 10, line 45- column 11, line 13).

It would have been prima facie obvious to modify the endogenous molecule of Low et al as combined supra by further conjugation to a bacterial targeting antibody according to Kim because Kim teach that anti-bacterial antibody conjugates provides for concentrated localized delivery of the conjugate to the bacterium.

Status of the Claims

Claims 36-38 and 42 are withdrawn from consideration. Claims 1-8, 21-29 and 32-35 stand rejected.

Conclusion

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia A. Duffy whose telephone number is 571-272-0855. The examiner can normally be reached on M-Th 6:30 am - 6:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's Supervisor Shanon Foley can be reached on 571-272-0898.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/Patricia A. Duffy/
Patricia A. Duffy, Ph.D.
Primary Examiner
Art Unit 1645